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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/584,411	05/31/2000	Richard A. Shimkets	15966-552 (Cura-52)	6088

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/584,411	SHIMKETS ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39,41-49 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39 41-49 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 39, 41 to 49 and 51 are pending in the instant application. Claims 40 and 50 have been canceled as requested by Applicant in the correspondence filed 29 January of 2004.

2) Any objection or rejection of record that is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4) Claims 39, 41 to 49 and 51 stand rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility for those reasons of record as applied to claims 39 to 51 in section 3 of the previous office action. The instant claims are drawn to an isolated polynucleotide encoding a polypeptide identified in the specification as "NOV11" (SEQ ID NO:22). As stated in the original rejection, the instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect.

Applicant has traversed this rejection on the premise that "there are numerous locations in the specification in which utility of the claimed invention is established". With the exception of those utilities described in the text on page 78 of the specification, the text referred to by Applicant does not describe even a single utility that is identified therein as being specific for an isolated polynucleotide encoding "NOV11" or an isolated polynucleotide complementary thereto. Every other utility referred to by Applicant is described in reference to "NOVX". The term "NOVX" encompasses no less than twenty three structurally and functionally unrelated proteins. The only common utilities for all of

these proteins and/or isolated polynucleotides encoding them are those general utilities applicable to all human proteins and their corresponding cDNAs. Such utilities as "chromosomal mapping", "cell and tissue typing" and "forensic biology" are not specific and substantial utilities for the claimed polynucleotide.

The employment of a protein of the instant invention, or a nucleic acid encoding that protein, as a chromosomal marker, tissue specific marker or forensic marker is not a substantial or specific utility for that protein or polynucleotide. All cDNAs can be employed as chromosomal markers and to detect "related" polynucleotides in a sample. All human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. It can be alleged that any protein that is expressed in a tissue specific manner can be employed to detect the tissue in which it is expressed in a sample. Alternately, a human protein that is expressed ubiquitously can be employed to detect the presence of any human tissue in a sample. Such utilities are analogous to the assertion that a particular polynucleotide or protein can be employed as a molecular weight marker, which is neither a specific or substantial utility.

One could just as readily argue that any purified compound having a known structure could be employed as an analytical standard in such processes as nuclear magnetic resonance (NMR), infrared spectroscopy (IR), and mass spectroscopy as well as in polyacrylamide gel electrophoresis (PAGE), high performance liquid chromatography (HPLC) and gas chromatography. None of these processes could be practiced without either calibration standards having known molecular structures or, at least, a range of molecular weight markers having known molecular weights. One could further extrapolate upon this premise by asserting that any item having a fixed measurable parameter can be employed to calibrate any machine or process which measures that parameter. For example, any item having a constant mass within an acceptable range can be employed to calibrate a produce scale in a grocery store. The calibration of produce scales is certainly an important function since most states require produce scales to be calibrated and certified. Therefore, to accept Applicant's arguments that any nucleic acid encoding any protein of human origin is useful as a marker would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object. It was just such applications that the court appeared to be referring to when it expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)). Because the steroid compound which was the subject of that decision had a known structure and molecular weight it could have readily been employed as a molecular standard at that time. Further, because that compound was a hydrocarbon it certainly could have been employed in the well known process of

combustion for purposes of lighting and/ or the generation of heat. The generation of heat by combustion of hydrocarbons certainly was and remains an important process. Irrespective of such obvious utilities, the court still held that the compound produced by the process at issue in *Brenner v. Manson* did not have a specific and substantial utility.

To grant Applicant a patent encompassing an isolated polynucleotide encoding a naturally occurring human protein of as yet undetermined biological significance would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" *(Brenner v. Manson, Ibid)*. To grant Applicant a patent on the claimed polynucleotide based solely upon an assertion that it can be employed as a chromosomal marker or that the protein encoded thereby can be employed as a tissue marker is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted and would be no different than granting a patent on the process disputed in *Brenner v. Manson* on the premise that the steroid produced thereby was useful as an analytical standard or as a combustible fuel source.

The alleged utilities described on pages 77 to 79 of the instant specification are utilities for Heregulin, tenascins, neurestins. As stated in the original rejection, the evidence of record clearly supports the conclusion that "NOV11" is not a neurestin, a tenascin or Heregulin, and, because the overall structural differences between "NOV11" and all known members of the neurestin, tenascin and Heregulin families greatly exceed

the similarities, one of ordinary skill would not reasonably believe that "NOV11" has the same range of biological activities and utilities as the members of those protein families.

Applicant has further traversed this rejection on the premise that an elevated level of expression of NOV11 in specific tissues is diagnostic for the presence of cancer in those tissues. Applicant relies upon the evidence provided in Table 4 beginning on page 173 of the instant specification. The data contained therein does not support any conclusion regarding the diagnostic utility of "NOV11". For example, "NOV11" is expressed in whole brain at a level of 32.5% of a reference value whereas it is expressed in various glioma and CNS cell lines at levels of 3.0%, 0.1%, 36.1%, 48.3%, 50.3%, 100.0%, 41.5% and 8.7%. Such data does not support a conclusion that one can diagnose the presence of a brain cancer by measuring the expression level of "NOV11" in a CNS sample.

Further, a brief search of the art for the terms "U87-MG" and "SW1783" has shown that these are neuronal cell lines that are known and used in the art. Therefore, the description of these cell lines as "tumor samples" on page 168 of the instant specification is not technically accurate. It appears that all of the data described in Table 4 of the instant specification appears to have been derived from cell lines of cancerous origin and from "normal tissue". A cell line, by its very nature, differs from the cell type from which it was derived in at least three very fundamental aspects. First, a cell line is usually derived from a population of cancerous cells which, by definition, proliferate in a manner which distinguishes them from their tissue of origin. One would reasonably expect the oncogenic process leading to the transformation of a cell into a cancer cell would result in some alteration in the level and type of proteins expressed by

that cell. Second, cell lines are derived from cancer cells through a process of immortalization. One of ordinary skill in the art of cell biology knows very well that the majority of primary cancer cells are not immortal and can not be immortalized. Those that are immortalized are often made so by extensive manipulative processes such as through the introduction of agents like the Epstein-Barr Virus (EBV). One of ordinary skill would understand that any process leading to the immortalization of a cancer cell into the progenitor of a cell line would also result in a significant alteration in the level and type of proteins expressed by that cell. Whereas it is well known that the transformation of a "normal" cell into a cancer cell can result from an alteration of a single gene, the process of immortalization appears to be much more complex and poorly understood, and probably has a more profound effect on the spectrum of proteins expressed by a cell, as evidenced by the aneuploidy usually observed in such cells. Finally, a "normal" cell *in vivo* grows in an environment which is substantially different from the *in vitro* environment of the cell line. One of ordinary skill would reasonable expect that simply changing the environment in which a cell is grown would result in a substantial alteration in the level and type of proteins expressed by that cell. Therefore, one of ordinary skill in art of molecular biology would not reasonably conclude that the observed difference between the level of expression of a protein of the instant invention in certain, but not all, cell lines originating from brain and that level of expression observed in "normal brain" supports a *prima facie* utility for that protein as a cancer marker.

5) Claims 39, 41 to 49 and 51 also stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a

credible substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

6) Applicant's arguments filed 29 January of 2004 have been fully considered but they are not persuasive for those reasons given above.

7) **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
PRIMARY EXAMINER
GROUP 1800